

What is claimed is

1. A method of treating, preventing or reducing the risk of developing a depressive disorder in a subject in need thereof, comprising: administering a depressive-disorder-effective amount of a composition to an area of skin of the subject for delivery of a steroid in the testosterone synthetic pathway to blood serum of the subject, wherein the composition comprises:

- (a) about 0.01% to about 70% of the steroid in the testosterone synthetic pathway;
- (b) about 0.01% to about 50% penetration enhancing agent;
- (c) about 0.01% to about 50% thickening agent; and
- (d) about 30% to about 98% lower alcohol;

wherein the composition is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10 µg per day of the steroid to the blood serum of the subject; and the percentages are on a weight to weight basis of the composition.

2. The method of claim 1, wherein the steroid in the testosterone synthetic pathway comprises about 0.1% to about 10% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, or derivative thereof.

3. The method of claim 1, wherein the steroid in the testosterone synthetic pathway comprises about 1% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, or derivative thereof.

4. The method of claim 2, wherein the penetration enhancing agent comprises about 0.1% to about 5% of isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of

polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, or terpene.

5        5.        The method of claim 4, wherein the penetration enhancing agent is isopropyl myristate.

6.        The method of claim 2, wherein the thickening agent comprises about 0.1% to about 5% polyacrylic acid.

7.        The method of claim 6, wherein the thickening agent comprises about 0.9 % polyacrylic acid.

10       8.        The method of claim 6, wherein the polyacrylic acid is carboxypolymethylene.

9.        The method of claim 2, wherein the lower alcohol comprises about 45% to about 90% ethanol or isopropanol.

10.       The method of claim 2, wherein the composition further comprises about 0.1% to about 10% sodium hydroxide.

15       11.       The method of claim 2, wherein the composition weighs equal to or less than about 100 grams.

12.       The method of claim 2, wherein the composition weighs about 1.0 grams to about 10 grams.

20       13.       The method of claim 2, wherein the composition weighs about 2.5 grams to about 7.5 grams.

14.       The method of claim 2, wherein the composition weighs about 5.0 grams.

15.       The method of claim 2, wherein the composition is capable of releasing the testosterone after applying the composition to the skin at a rate and duration that achieves circulating serum concentration of the testosterone greater than about 400 ng testosterone per

dl serum during a time period beginning about 2 hours after administration and ending about 24 hours after administration.

16. The method of claim 15, wherein the serum testosterone concentration is maintained between about 400 ng testosterone per dl serum to about 1050 ng testosterone per  
5 dl serum.

17. The method of claim 2, wherein for each about 0.1 gram per day application of the composition to the skin, an increase of at least about 5 ng/dl in serum testosterone concentration results in the subject.

18. The method of claim 2, wherein the composition is provided to the subject for  
10 daily administration in about a 0.1 g to about a 10 g dose.

19. The method of claim 2, wherein the amount of the composition is a 5 g dose delivering about 5 mg to about 500 mg of testosterone to the skin.

20. The method of claim 2, wherein the amount of the composition is a 7.5 g dose delivering about 7.5 mg to about 750 mg of testosterone to the skin.

15 21. The method of claim 2, wherein the amount of the composition is a 10 g dose delivering 10 mg to about 1000 mg of testosterone to the skin.

22. The method of claim 2, wherein the composition is provided to the subject in one or more packets.

23. The method of claim 22, wherein the packet comprises a polyethylene liner  
20 between the composition and inner surface of the packet.

24. The method of claim 2, wherein the composition is provided as a separate component to a kit.

25. The method of claim 2, wherein the subject has a pretreatment serum testosterone concentration less than about 300 ng/dl.

26. The method of claim 25, wherein after at least about 30 days of daily administration serum testosterone concentration in the subject is at least about 490 ng/dl to about 860 ng/dl.

27. The method of claim 25, wherein after at least about 30 days of daily administration total serum androgen concentration in the subject is greater than about 372 ng/dl.

28. The method of claim 2, wherein the composition is administered once, twice, or three times daily for at least about 7 days.

29. A method of treating, preventing or reducing the risk of developing a depressive disorder in a subject in need thereof, comprising: administering to the subject:

(a) an amount of a composition comprising:

(i) about 0.01% to about 70% steroid in the testosterone synthetic pathway;

(ii) about 0.01% to about 50% penetration enhancing agent;

(iii) about 0.01% to about 50% thickening agent; and

(iv) about 30% to about 98% lower alcohol; and

(b) an amount of a therapeutic agent comprising an antidepressant agent, an inhibitor of the synthesis of sex hormone binding globulin, or an estrogenic hormone; wherein

the composition is administered to an area of skin of the subject for delivery of the steroid to blood serum of the subject, and is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10 µg per day of the steroid to the blood serum of the subject, and the percentages are on a weight to weight basis of the composition; and

the amount of the composition and the amount of the therapeutic agent together make a depressive-disorder-effective amount.

30. The method of claim 29, wherein the steroid in the testosterone synthetic pathway comprises about 0.1% to about 10% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, or derivative thereof.

31. The method of claim 29, wherein the steroid in the testosterone synthetic pathway comprises about 1% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, prodrug, or derivative thereof.

32. The method of claim 29, wherein the penetration enhancing agent comprises about 0.1% to about 5% of isostearic acid, octanoic acid, lauryl alcohol, ethyl oleate, isopropyl myristate, butyl stearate, methyl laurate, diisopropyl adipate, glyceryl monolaurate, tetrahydrofurfuryl alcohol, polyethylene glycol ether, polyethylene glycol, propylene glycol, 2-(2-ethoxyethoxy) ethanol, diethylene glycol monomethyl ether, alkylaryl ethers of polyethylene oxide, polyethylene oxide monomethyl ethers, polyethylene oxide dimethyl ethers, dimethyl sulfoxide, glycerol, ethyl acetate, acetoacetic ester, N-alkylpyrrolidone, or terpene.

33. The method of claim 32, wherein the penetration enhancing agent is isopropyl myristate.

34. The method of claim 29, wherein the thickening agent comprises about 0.1% to about 5% polyacrylic acid.

35. The method of claim 34, wherein the thickening agent comprises about 0.9 % polyacrylic acid.

36. The method of claim 34, wherein the polyacrylic acid is carboxypolymethylene.

37. The method of claim 29, wherein the lower alcohol comprises about 45% to about 90% ethanol or isopropanol.

38. The method of claim 29, wherein the composition further comprises about 0.1% to about 10% sodium hydroxide.

5 39. The method of claim 29, wherein the composition and the therapeutic agent are provided as separate components to a kit.

40. The method of claim 29, wherein the composition and the therapeutic agent are administered substantially simultaneously, or sequentially.

10 41. The method of claim 29, wherein the therapeutic agent is administered orally; percutaneously, intravenously, intramuscularly, or by direct absorption through mucous membrane tissue.

42. A pharmaceutical composition for administration to skin of a subject, comprising:

- 15 (i) about 0.01% to about 70% steroid in the testosterone synthetic pathway;
- (ii) about 0.01% to about 50% penetration enhancing agent;
- (iii) about 0.01% to about 50% thickening agent;
- (iv) about 30% to about 98% lower alcohol; and
- (v) a therapeutic agent comprising an antidepressant agent, an inhibitor of the synthesis of sex hormone binding globulin, or an estrogenic hormone; and

20 wherein

the composition is capable of being administered to an area of skin of the subject for delivery of the steroid in the testosterone synthetic pathway and the therapeutic agent to blood serum of the subject, and is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10 µg per day of the

steroid to the blood serum of the subject, and the percentages are on a weight to weight basis of the composition; and

the amount of the steroid and the amount of the therapeutic agent together make a depressive-disorder-effective amount.

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